

AMENDMENTS TO THE CLAIMS

Claim 1 (Currently Amended) A transgenic mouse or rat ~~non-human mammal~~ comprising a foreign DNA,

the foreign DNA having a DNA which is located under the control of a type II collagen promoter,

wherein the DNA ~~which~~ is selected from the group consisting of an MHC class II transactivator gene, an active region of the MHC class II transactivator gene, and a mutant of the MHC class II transactivator gene, the mutant has ~~(having a master switch function for controlling an expression of the MHC class II genes) and which is located under the control of a type II collagen promoter~~

wherein pathologic conditions of human rheumatoid arthritis are presented by twice or more administration of type II collagen in which a dose of the type II collagen for each administration is set to 0.01 mg to 0.05 mg.

Claim 2 (Currently Amended) The transgenic mouse or rat ~~non-human mammal~~ according to claim 1, wherein the foreign DNA comprises a type II collagen enhancer.

Claims 3 and 4: Cancelled

Claim 5 (Currently Amended) The transgenic mouse or rat ~~non-human mammal~~ according to claim 1, which shows the following pathologic conditions (1) to (6) ~~wherein the pathologic condition of human rheumatoid arthritis is a pathologic condition showing one or more of the following (1) to (7):~~

- (1) Joint swelling is observed ~~in three places or more~~ in the whole body;
- ~~(2) Symmetry joint swelling is observed;~~
- ~~(23)~~ Joint swelling lasting for a week or more is observed;
- (34) Destruction, ankylosis, or deformity of bones in the extremities is observed;
- (45) Infiltration of lymphoid cells is observed;
- (56) Cartilage destruction and bone destruction due to formation of granulation tissue are observed; and

(67) Joint deformity progresses through early stage (stage I) and moderate stage (stage II).

Claims 6-10: Canceled

Claim 11 (Withdrawn): A method of producing a transgenic non-human mammal, the method comprising a step of:

introducing a foreign DNA into a cell in an early stage, the foreign DNA having a DNA which is selected from the group consisting of an MHC class II transactivator gene, an active region of the MHC class II transactivator gene, and a mutant of the MHC class II transactivator gene (having a master switch function for controlling an expression of the MHC class II genes) and which is located under the control of a type II collagen promoter.

Claim 12 (Withdrawn): The method of producing a transgenic non-human mammal according to claim 11, wherein the foreign DNA comprises a type II collagen enhancer.

Claim 13 (Withdrawn): An expression vector comprising:

a type II collagen promoter;

a DNA sequence located downstream from the type II collagen promoter and selected from the group consisting of a MHC class II transactivator gene, an active region of the MHC class II transactivator gene, and a mutant of the MHC class II transactivator gene (having a master switch function for controlling an expression of the MHC class II genes); and

a type II collagen enhancer.

Claim 14 (Withdrawn): A screening method of a drug for human rheumatoid arthritis, the method comprising the following steps (a) to (c):

(a) inducing pathologic conditions of human rheumatoid arthritis in the transgenic non-human mammal described in any of claims 1 to 10;

(b) administering a test substance to the transgenic non-human mammal; and

(c) examining whether symptoms characteristic of human rheumatoid arthritis is relieved.

Claim 15 (Withdrawn): The screening method according to claim 14, wherein the step (c) determines whether one or more of the symptoms selected from the following (1) to (10) is relieved:

- (1) Joint swelling is observed in three places or more in the whole body;
- (2) Symmetry joint swelling is observed;
- (3) Joint swelling lasting for a week or more is observed;
- (4) Destruction, ankylosis, or deformity of bones in the extremities is observed;
- (5) Infiltration of lymphoid cells is observed;
- (6) Cartilage destruction and bone destruction due to formation of granulation tissue are observed;
- (7) Joint deformity progresses through early stage (stage I) and moderate stage (stage II);
- (8) Angiitis is observed;
- (9) Interstitial pneumonia, pleuritis, and the like, are observed; and
- (10) Anemia is observed.

Claim 16 (Withdrawn): A screening method of a drug for human rheumatoid arthritis, the method comprising the following steps (A) to (C):

- (A) preparing a test group and a control group, the test group comprising one individual or more of the transgenic non-human mammal described in any of claims 1 to 10 in which a pathologic condition of human rheumatoid arthritis is induced;
- (B) administering a test substance to each individual of the test group; and
- (C) comparing the degree of symptoms characteristic of human rheumatoid arthritis between the test group and the control group.

Claim 17 (Withdrawn): The screening method according to claim 16, wherein the step (C) compares one or more of the symptoms selected from the following (1) to (10) between the test group and the control group:

- (1) Joint swelling is observed in three places or more in the whole body;
- (2) Symmetry joint swelling is observed;
- (3) Joint swelling lasting for a week or more is observed;
- (4) Destruction, ankylosis, or deformity of bones in the extremities is observed;

- (5) Infiltration of lymphoid cells is observed;
- (6) Cartilage destruction and bone destruction due to formation of granulation tissue are observed;
- (7) Joint deformity progresses through early stage (stage I) and moderate stage (stage II);
- (8) Angiitis is observed;
- (9) Interstitial pneumonia, pleuritis, and the like, are observed; and
- (10) Anemia is observed.